Journal of Regenerative Biology and Medicine

ISSN: 2582-385X
Timmons RB, et al., 2020- J Regen Bio Med
Research Article

Retrospective Chart Review of Cryopreserved Amniotic Membrane for Knee Pain

Ruben Berrocal Timmons[1*], Neal E. Fearnot[2] and Lori Deneke Bane[3]

[1]Regenerative Medicine and Pain Medicine Physicians, 3406 Santa Rosa Drive, Gulf Breeze, FL, USA

[2]Cook Biotech Incorporated, 1400 Cumberland Avenue, West Lafayette, IN, USA

[3]Regenerative Medicine and Pain Medicine Physicians, 3406 Santa Rosa Drive, Gulf Breeze, FL, USA

[*]**Corresponding Author:** Ruben Berrocal Timmons, Regenerative Medicine and Pain Medicine Physicians, 3406 Santa Rosa Drive, Gulf Breeze, FL, USA

Received Date: 11-11-2020
Published Date: 12-11-2020

Abstract

Objective: Treatment of joint pain with injection of amniotic membrane has not been adequately studied. This study retrospectively reviewed Visual Analog Scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and analgesic usage data from patients treated with the injection of cryopreserved amniotic membrane (CAM) in their knees to determine the impact of treatment on patients' pain, quality of life, and analgesic usage.

Methods: Chart review was conducted on 40 patients. Institutional Review Board (IRB) approval was obtained prior to initiation of the project. The membrane was utilized as per the FDA guidance of 21CFR1271. Retrospective data, including demographics, medical history, pain score, quality of life score, analgesic usage and adverse events, were collected from their medical records for each consenting patient through 6 months after CAM injection.

Results: A total of 40 patients were considered in the final analysis. Mean VAS for pain level improved from 7.0 to 2.6 ($p<0.001$). WOMAC daily activity function score improved from a mean score of 52 to 28 ($p<0.001$). Opioid and non-steroidal anti-inflammatory drug (NSAID) usage decreased from 97% to 25% ($p<0.001$). No adverse events were reported.

Conclusion: Mean values for VAS and WOMAC scores significantly improved at all time points and the number of patients who used analgesics decreased as compared to baseline. CAM injection into painful knee joints decreases pain, improves physical function, and decreases the use of analgesics in the absence of adverse events.

Keywords: Amnion; Amniotic Membrane; Joint Pain; Knee Pain; Regenerative Medicine.

Introduction

Pain associated with osteoarthritis (OA) persists as a significant debilitating problem affecting an estimated 54.4 million Americans and is a leading cause of

Citation: Timmons RB, Fearnot NE and Bane LD. Retrospective chart review of Cryopreserved Amniotic Membrane for knee pain. J Regen Biol Med. 2020;3(1):1-10.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-3(1)-047

disability [1]. OA symptoms include chronic inflammation, oxidative stress, activation of matrix metalloproteases (MMP), and loss of proteoglycan that ultimately lead to cartilage degradation [2].

The average total cost for a total knee replacement in the United States is approximately $57,000 including hospital charges as well as anesthesiologist's and surgeon's fees, but the cost varies by city [3]. This does not include time off work, assistance during recovery, physical therapy and post-operative medication. Hospital costs for total knee replacements in 2012 totaled $28.5 billion [4]. OA has increased from a rank of 31 to a rank of 25 in the list of leading causes of Disability-Adjusted Life-Years (DALYs) from 1990 to 2016 [5]. Twenty-five percent (25%) of patients with knee and hip OA are unable to perform key daily activities and 40% relate fair to poor overall health. Many qualify as disabled [6].

Existing treatments for joint pain are limited to medical management, injection therapy and surgery. A Denmark study revealed that total knee replacement (TKR) plus non-surgical treatments such as exercise, education, diet, insoles, and pain medication was not more cost-effective over 24 months than simply using non-surgical treatments alone for patients with moderate to severe knee OA [7]. However, medications that may aid in reducing pain carry with them a significant morbidity, social concern, and medication dependency.

Opioids are commonly prescribed for adults with OA even though physical activity alone may reduce pain and improve physical function by an estimated 40% [1]. Seventy percent (70%) of deaths due to drug overdose in 2018 involved an opioid or synthetic opioid [8]. Deaths from opioid overdose tripled from 2000 to 2016 [9]. Health care providers confront the burden and cost of monitoring chronic patient opioid use while preventing abuse. There are nearly 1000 daily emergency room visits secondary to substance abuse disorders. Opioid and substance abuse disorders are said to involve 2.1 million people in the United States [10].

Non-steroidal anti-inflammatory drugs (NSAIDs), as well as acetaminophen, are accepted as the first line of treatment in patients with joint pain [11]. However, NSAIDs may cause added comorbidities such as gastrointestinal, kidney, cardiovascular, and hepatic complications. Overdose of these commonly prescribed and over the counter first-line medications, such as NSAIDs, result in over 100,000 hospitalizations, 16,000 deaths and annual costs of $2 billion [12] Of added concern during the COVID-19 pandemic, there is speculation that NSAID use induces cytokine storms which may result in prolonged illness and more severe respiratory and/or cardiac complications [13].

Intra-articular steroid injections are intended to relieve joint pain by reducing inflammation. However, in recent reviews, many patients had problems after injections including worsening pain and breakdown of cartilage in the joint [14]. Other side effects include weight gain, diabetes exacerbations, cataracts, osteoporosis, and increased risk of infection. Biologics and Disease-Modifying Anti-Rheumatic Drugs (DMARDs) have also been used in the treatment of joint

Citation: Timmons RB, Fearnot NE and Bane LD. Retrospective chart review of Cryopreserved Amniotic Membrane for knee pain. J Regen Biol Med. 2020;3(1):1-10.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-3(1)-047

pain. However, they also carry risks which include, but are not limited to, cancer, pneumonia, tuberculosis and death [15].

Surgery, opioids, NSAIDs, steroids, biologics and DMARDs for treatment of chronic pain often have limited effect on pain as well as associated side effects. Clearly, alternative approaches to relief of joint pain are needed.

Background on Amniotic Membrane

Amniotic membrane (AM) is obtained under the requirements and standards of the Human Cellular and Tissue-Based Product (HCT/P) regulations. The methodology for preparing amniotic membrane may vary from manufacturer to manufacturer in terms of quality which in turn may affect clinical results.

AM from healthy, live births contains a multitude of cytokines. AM is characterized by structural proteins such as collagen, glycoproteins, proteoglycans, and growth factors. This natural scaffold is a crucial support to the biochemical and biomechanical processes occurring at a cellular level. Wound healing, guided cell migration, and tissue morphogenesis are a few of the attributes associated with the extracellular matrix (ECM). Some of the cytokines and growth factors identified include VEGF, IL-4, IL-10, PGE2, and TIMPs. These cytokines also provide potent anti-inflammatory and anti-fibrotic effects on joint disease. PGE2 has been demonstrated to convert inflammatory macrophages to anti-inflammatory macrophages [16-30].

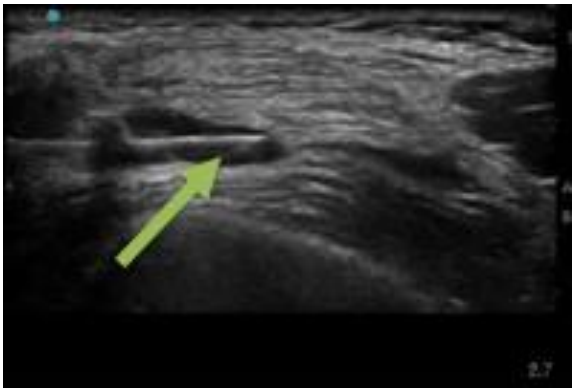
AM has been utilized in multiple applications which include burns, chronic ulcers, pterygium, as well as orthopedic and podiatric surgeries [17, 31] Besides exhibiting metabolic processes such as collagen synthesis, AM also reduces pain, prevents fibrosis, and has antibacterial properties [31-35].

Background on Ultrasound-Guided Knee Injection Utilizing the Lateral Suprapatellar Approach

After patient education and consent for therapy, the patient was placed in the supine position with the knee in extension. The lateral aspect was prepped with Betadine ×3 and sterile drapes were applied. The ultrasound probe was placed over the superior aspect of the patella to visualize the bony structures, followed by the application of topical anesthetic ethyl chloride spray. The CAM, which comes in a 20-gauge 1.5-inch needle maintained at -80 °C, had been gradually thawed at room temperature. Following adequate thawing, a 5 ml syringe filled with sterile preservative-free normal saline was then attached to the CAM-prepared needle. The needle was directed into the suprapatellar bursa under ultrasound visualization, where the CAM and normal saline were injected under direct visualization (Figure 1).

Citation: Timmons RB, Fearnot NE and Bane LD. Retrospective chart review of Cryopreserved Amniotic Membrane for knee pain. J Regen Biol Med. 2020;3(1):1-10.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-3(1)-047

Figure 1: Ultrasound-guided suprapatellar bursa injection. The needle is visualized in the suprapatellar bursa, entering from the left.



The post-procedure evaluation involved monitoring the patient for alertness, pain, stable vital signs (blood pressure and heart rate), and unchanged neurologic status at 15 minutes and 60 minutes. Postoperative instructions were provided, and the patient was discharged in stable condition.

While CAM injections in the knee are routine clinical practices at this institution, outcomes have not been previously reported with this particular product. Patients receiving CAM for joint pain have previously failed conservative and conventional therapies which include, but are not limited to, pharmacological management and physical therapy. As a result of inadequate improvement of pain, it is deemed medically necessary to proceed with minimally invasive interventional treatment.

Materials and Methods

Cryopreserved amniotic membrane (CAM) (VIM® Injectable Amnion, Cook Biotech Incorporated, West Lafayette, IN, USA) is an aseptically processed tissue that meets the requirements for HCT/P as defined by US FDA 21 CFR Part 1271. All tissues were obtained from consenting donors undergoing elective Caesarian sections that were properly screened and tested for infectious diseases. The product was cryopreserved in 10% dimethyl sulfoxide (DMSO) solution and provided within a 20-gauge needle retaining much of its original matrix microstructure and cytokine profile. The CAM was minimally manipulated and used homologously. The tissue was processed to preserve the native biological component and structure of the ECM. Therefore, the membrane may serve as a protective barrier or cushion when tunneled into or injected over the damaged joint.

This chart review project was conducted at a single site in the United States from March 2018 through October 2019. The medical charts of 40 consenting adult subjects with knee pain, previously treated with CAM, were reviewed for the following metrics: Visual Analog Scale (VAS) pain scores, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) daily activity function, opioid usage, NSAID usage, and adverse events under an Institutional Review Board (IRB)-approved protocol. Each patient who agreed to participate signed an IRB-generated informed consent document to allow their de-identified data to be used for

Citation: Timmons RB, Fearnot NE and Bane LD. Retrospective chart review of Cryopreserved Amniotic Membrane for knee pain. J Regen Biol Med. 2020;3(1):1-10.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-3(1)-047

this study. Volunteers were recruited through word of mouth.

The study size was arrived at using acceptable standards of study samples that range between 20 - 40 patients. The pain was evaluated using the VAS as assessed by the patient at baseline, 1 hour, 24 hours, 1 week, 2 weeks, 8 weeks, 12 weeks and 6 months, consistent with the standard patient follow-up schedule for this review. Pain, stiffness and physical function were assessed using the WOMAC questionnaire as completed by the patient at baseline, 2 weeks, 8 weeks, 12 weeks and 6 months. Use of opioid medications and NSAIDs were recorded at baseline, 24 hours, 1 week, 2 weeks, 8 weeks, 12 weeks and 6 months.

Onsite and remote monitoring was conducted to verify the data submitted against site records. Any discrepancies found during the on-site monitoring visit were resolved through a formal query process before final data analyses. Statistical analysis was performed (SYSTAT 13) using a repeated-measures analysis of variance. A p-value of <0.05 was prospectively determined to represent significance. (Ho: $\mu1=\mu2=\mu n$).

Ethical considerations

This project was conducted by the ethical principles that have their origin in the Declaration of Helsinki. The project plan and any amendments were submitted to the IRB for approval before implementation. All patients in this project were provided with an IRB-approved consent form describing this project and providing sufficient information for patients to make an informed decision about their participation in this project. Written consent was given by each patient before any data collection.

Patient Population

This project enrolled a total of 40 patients who were treated with CAM for knee pain. These patients failed conservative and conventional therapies which include pharmacological and physical therapy with the inadequate improvement of pain, making it medically necessary to proceed with interventional treatment. All patients who met the criteria were invited to participate in the project, and the first 40 consecutive patients who agreed were enrolled. The patient selection criteria are listed below.

Inclusion Criteria:

1. Prior treatment with CAM for the management of knee pain.

Exclusion Criteria:

1. Age < 18 years
2. Unwilling or unable to give informed consent for data use.

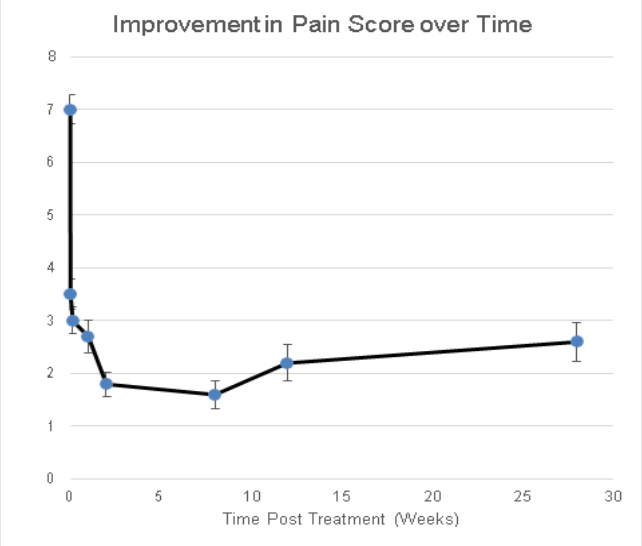
Consenting patients were able to withdraw from the project at any time without penalty.

Results

Medical records for 40 patients provided substantially complete data regarding demographics and outcomes. Mean age was 66.0 ± 10.1 years, (range 47-93). Mean BMI 30.5 ± 6.3 (range 19.8-50.2). Of the 40 knee subjects, 18 were female and 22 were male. VAS-measured pain scores improved from 7.0 to 2.6 over 6 months ($p<0.001$) (Figure 2).

Citation: Timmons RB, Fearnot NE and Bane LD. Retrospective chart review of Cryopreserved Amniotic Membrane for knee pain. J Regen Biol Med. 2020;3(1):1-10.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-3(1)-047

Figure 2: Mean VAS pain scores before and after treatment, with standard errors.

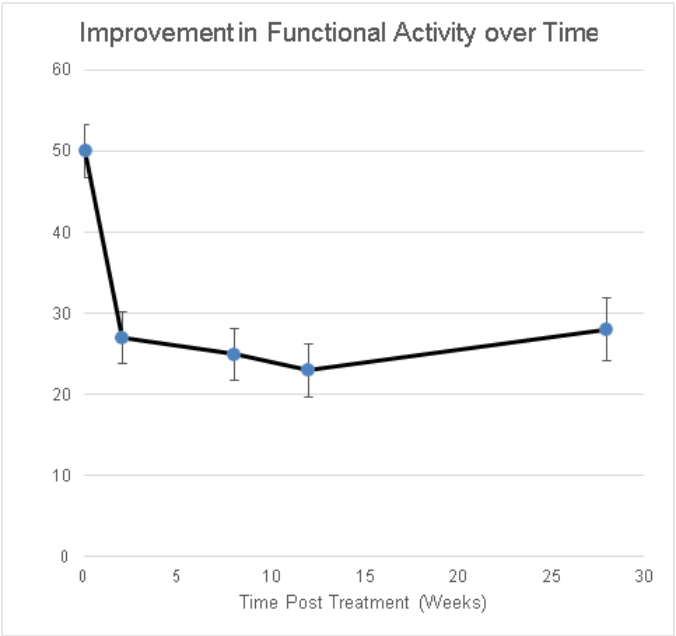


Paired T testing indicates:

- VAS at Time-0 (Pre) significantly greater than at all later times.
- VAS at 1-Hour Significantly greater than at Weeks 2, 8 and 12.
- VAS at Day-1 Significantly greater than at Weeks 2 and 8.
- VAS at Week-1 Significantly greater than Week 2.

WOMAC-measured physical function scores improved from 50.0 to 23 over 12 weeks and 28 at 6 months ($p<0.001$) (Figure 3).

Figure 3: Mean WOMAC scores before and after treatment, with standard error.



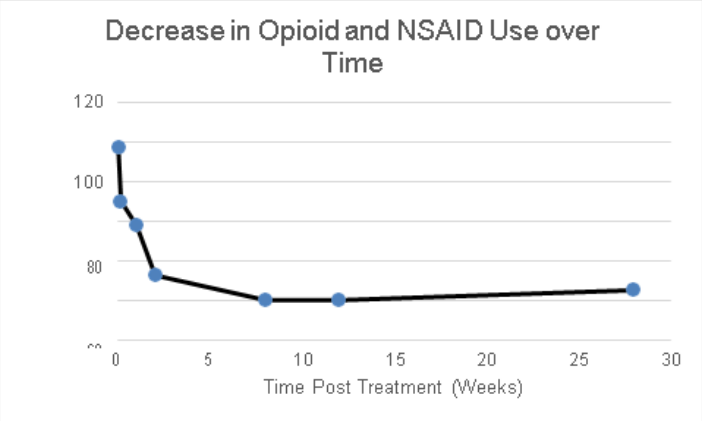
Citation: Timmons RB, Fearnot NE and Bane LD. Retrospective chart review of Cryopreserved Amniotic Membrane for knee pain. J Regen Biol Med. 2020;3(1):1-10.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-3(1)-047

Paired T testing indicates:

- WOMAC is significantly improved at all post-procedure follow-up times compared to T=0.
- WOMAC is not significantly different between post-procedure follow-up times.

Paired t testing on the dosage values of pain medicine given at baseline versus those given at 6 months demonstrated that opioid and NSAID usage decreased significantly by 58.6% (p=0.001). At 6 months, 75% of patients were on no pain medication at all (Figure-4).

Figure 4: Opioid/NSAID use before and after treatment.



Summary of Opioid and NSAID usage by patients is given below:

- One patient received neither opioids nor NSAIDs at any time during the study (#38).
- Two patients received only opioids (#30 and #31).
- Thirty-four patients received only NSAIDs.
- Three patients received both opioids and NSAIDs (#13, #20 and #22).
- Twenty-five patients took neither opioids nor NSAIDS after Week 1.

No adverse events were reported throughout 6 months. All three outcome measures (VAS, WOMAC, analgesic usage) demonstrated significant improvement. Extended follow-up averaged over 365 days. Only one patient required surgical intervention within the 6 months, however, that patient was able to postpone knee surgery for 3 months post-injection. Two patients fell and re-injured their knees before their 6-month follow-ups which resulted in recurrent knee pain and the patients were given 2nd injections. The patient with a BMI of 50.2, who ambulated by motorized wheelchair, was able to stand without pain for the first time in 20 years immediately following his injection. However, due to his morbid obesity, he remained minimally ambulatory. He did, however, experience significantly decreased pain at rest following his injection.

Citation: Timmons RB, Fearnot NE and Bane LD. Retrospective chart review of Cryopreserved Amniotic Membrane for knee pain. J Regen Biol Med. 2020;3(1):1-10.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-3(1)-047

Discussion

A chart review of 40 patients with knee pain revealed the clinical benefits of injecting CAM. Improvement in pain, physical function, opioid use and NSAID use began promptly after treatment and was sustained over at least 6 months. According to the Centers for Disease Control, there is a national epidemic of opioid dependency, overdose and abuse, leading to reluctance in prescribing and difficulty in managing patients on opioids. CAM offers an important alternative [7]. Likewise, the decreased use of NSAIDs will also greatly reduce the morbidity associated with chronic use of NSAIDs.

Before treatment, patients were physically deconditioned secondary to their pain, complicating recovery and functional restoration. Excessive BMI also may have contributed to the increase in knee osteoarthritis pathology. Remodeling of cartilage following amnion injection probably requires an appropriate environment of cells and factors, scaffolds, oxygen tension, and mechanical force [36]. Therefore, patients were counseled on diet, physical therapy and a gradual return to physical activity as critical adjunctive measures for achieving improvement in daily living metrics.

CAM product and injection costs range from $2500 to $5000 per knee. While less expensive than knee replacement, CAM is more costly than a steroid injection, however, it is free of side effects as compared to steroids. If pain relief from a CAM injection extends beyond 6 months, CAM requires fewer procedures than steroids or commercial hyaluronic acid preparations which require multiple injections over a short amount of time. Since the costs of the interventional procedure and subsequent follow-up office visits are identical, it is plausible that the overall cost of patient management will be reduced with CAM. At this time, it is unknown whether subsequent CAM injections may improve the length of success. Also, from our experience treating knees, it is expected that the same result may be obtained in other joints and clinical studies would be warranted.

While this chart review supports the safety and effectiveness of CAM, chart review inherently has limitations related to data robustness. For example, treatment was not prospectively randomized against control depicting the current standard of care. The possibility for bias is also a consideration given that the data were collected by the same physician performing the injections; however, an external review was performed to corroborate the data. Therefore, further research may provide additional confirmation regarding the longer-term outcome of pain relief, sustained functional activity, dependence on medications with known morbidity, and relative healthcare cost of treating these patients with advanced arthritic pain before knee replacement.

Conclusion

CAM injection reduces pain, physical disability, and analgesic usage in patients suffering from knee pain without adverse events. Patients treated with CAM were able to prevent or postpone the need for knee

Citation: Timmons RB, Fearnot NE and Bane LD. Retrospective chart review of Cryopreserved Amniotic Membrane for knee pain. J Regen Biol Med. 2020;3(1):1-10.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-3(1)-047

replacement and improve quality of life as well as reduce medication use, most notably opioid use. Given the improvement observed in patients suffering from OA with knee pain, CAM offers a superior advantage over common and conventional knee treatments and medications.

Acknowledgements

Cook Advanced Technology, Pratik Kalsaria, William Voorhees Ted Heise, Mike Otlewski.

References

1. Barbour KE, Helmick CG, Boring M, Brady TJ. Vital signs: prevalence of doctor-diagnosed arthritis and arthritis-attributable activity limitation—United States, 2013–2015. Mortal. Wkly. Rep. 2017;66(9):246.
2. Goldring MB. otero M. Inflammaion in osteoarthriis. Curr Opin Rheumatol. 2011;23:471r8.
3. Greengard S. Understanding knee replacement costs: What's on the bill. Healthline. com. Accessed October. 2017;2017.
4. Konopka JF, Lee YY, Su EP, McLawhorn AS. Quality-adjusted life years after hip and knee arthroplasty: health-related quality of life after 12,782 joint replacements. J Bone Joint Surg Br. 2018;3(3).
5. Murphy L, Helmick CG. The Impact of Osteoarthritis in the United States: A Population-Health PerspectiveA population-based review of the fourth most common cause of hospitalization in US adults. Orthop Nurs. 2012;31(2):85-91.
6. Begg S, et al. The Burden of Disease and Injury in the United States 1996. Popul. Health Metr. 2006.
7. Skou ST, et al. Cost-effectiveness of total knee replacement in addition to non-surgical treatment: a 2-year outcome from a randomised trial in secondary care in Denmark. Bmj Open. 2020;10(1).
8. Wilson N. Drug and opioid-involved overdose deaths—United States, 2017–2018. MMWR. MMWR Morb Mortal Wkly Rep. 2020;69.
9. Rudd RA, Aleshire N, Zibbell JE, Gladden RM. Increases in drug and opioid overdose deaths—United States, 2000–2014. MMWR Morb Mortal Wkly Rep. 2016;64(50 & 51):1378-82.
10. Volkow ND. America's addiction to opioids: Heroin and prescription drug abuse. Senate Caucus on International Narcotics Control. 2014;14:1-6.
11. Evidence-Based Update on Pain Management and NSAIDs." Pharmacy Times, Iroko Pharmaceuticals.2013, 1:12:41.
12. Timmons RB, Fearnot NE, Leckrone ME. Chart Review Study of Subjects Administered Amnionic Membrane for Treatment of Joint Pain. Curr Trends Biotechnol Pharm. 2018;12(3):212-7.
13. Viswanath A, Monga P. Working through the COVID-19 outbreak: rapid review and recommendations for MSK and allied heath personnel. J Clin Orthop Trauma.2020.
14. Kompel AJ, et al. Intra-articular corticosteroid injections in the hip and knee: perhaps not as safe as we thought? Radiology. 2019;293(3):656-63.
15. Timmons RB, Fearnot NE, Leckrone ME. Chart Review Study of Subjects Administered Amnionic Membrane for Treatment of Joint Pain. Curr Trends Biotechnol Pharm2018;12(3):212-7.
16. Koob TJ, et al. Biological properties of dehydrated human amnion/chorion composite graft: implications for chronic wound healing. Int Wound J. 2013;10(5):493-500.
17. Subach BR, Copay AG. The use of a dehydrated amnion/chorion membrane allograft in patients who subsequently undergo reexploration after posterior lumbar instrumentation. Adv Orthop. 2015;2015.
18. Hao Y, Ma DH, Hwang DG, Kim WS, Zhang F. Identification of antiangiogenic and antiinflammatory proteins in human amniotic membrane. Cornea. 2000;19(3):348-52.

Citation: Timmons RB, Fearnot NE and Bane LD. Retrospective chart review of Cryopreserved Amniotic Membrane for knee pain. J Regen Biol Med. 2020;3(1):1-10.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-3(1)-047

19. KIM JS, KIM JC, NA BK, JEONG JM, SONG CY. Amniotic membrane patching promotes healing and inhibits proteinase activity on wound healing following acute corneal alkali burn. Clin Exp Ophthalmol. 2000;70(3):329-37.
20. Riau AK, Beuerman RW, Lim LS, Mehta JS. Preservation, sterilization and de-epithelialization of human amniotic membrane for use in ocular surface reconstruction. Biomaterials. 2010;31(2):216-25.
21. Solomon A, et al. Suppression of interleukin 1α and interleukin 1β in human limbal epithelial cells cultured on the amniotic membrane stromal matrix. Br J Ophthalmol. 2001;85(4):444-9.
22. Koob TJ, Lim JJ, Zabek N, Massee M. Cytokines in single layer amnion allografts compared to multilayer amnion/chorion allografts for wound healing. J Biomed Mater Res B Appl Biomater. 2015;103(5):1133-40.
23. Shimmura S, Shimazaki J, Ohashi Y, Tsubota K. Antiinflammatory effects of amniotic membrane transplantation in ocular surface disorders. Cornea. 2001;20(4):408-13.
24. Koh JW, et. al. The expression of TIMPs in cryo-preserved and freeze-dried amniotic membrane. Curr Eye Res. 2007;32(7-8):611-6.
25. Grzywocz Z, et al. Growth factors and their receptors derived from human amniotic cells in vitro. Folia Histochem Cytobio 2014;52(3):163-70.
26. Koob TJ, et al. Angiogenic properties of dehydrated human amnion/chorion allografts: therapeutic potential for soft tissue repair and regeneration. Vasc. Cell. 2014;6(1):1-0.
27. Lindenmair A, et al. Intact human amniotic membrane differentiated towards the chondrogenic lineage. Cell Tissue Bank. 2014;15(2):213-25.
28. Fernandes JC, Martel-Pelletier J, Pelletier JP. The role of cytokines in osteoarthritis pathophysiology. Biorheology. 2002;39(1, 2):237-46.
29. Frisbie DD, Ghivizzani SC, Robbins PD, Evans CH, McIlwraith CW. Treatment of experimental equine osteoarthritis by in vivo delivery of the equine interleukin-1 receptor antagonist gene. Gene Ther. 2002;9(1):12-20.
30. Heusinkveld M, et al. M2 macrophages induced by prostaglandin E2 and IL-6 from cervical carcinoma are switched to activate M1 macrophages by CD4+ Th1 cells. J Immunol.;187:1157-65.
31. DeMill SL, et al. Safety analysis of cryopreserved amniotic membrane/umbilical cord tissue in foot and ankle surgery: a consecutive case series of 124 patients. Surg Technol Int. 2014;25:257-61.
32. Tao H, Fan H. Implantation of amniotic membrane to reduce postlaminectomy epidural adhesions. EUR SPINE J. 2009;18(8):1202-12.
33. Cargnoni A, et al. Amniotic membrane patching promotes ischemic rat heart repair. Cell Transplant. 2009;18(10-11):1147-59.
34. Kesting MR, et al. Cryopreserved human amniotic membrane for soft tissue repair in rats. Ann Plast Surg. 2008;60(6):684-91.
35. Mermet I, et al. Use of amniotic membrane transplantation in the treatment of venous leg ulcers. Wound Repair Regen. 2007;15(4):459-64.
36. Gaut C, Sugaya K. Critical review on the physical and mechanical factors involved in tissue engineering of cartilage. Regen Med. 2015;10(5):665-79.

Citation: Timmons RB, Fearnot NE and Bane LD. Retrospective chart review of Cryopreserved Amniotic Membrane for knee pain. J Regen Biol Med. 2020;3(1):1-10.
DOI: https://doi.org/10.37191/Mapsci-2582-385X-3(1)-047